Binding of Polychlorinated Biphenyls to the Aryl Hydrocarbon Receptor

Sherif A. Kafafi,[1] Hussein Y. Afeefy,[2] Ali H. Ali,[1] Hakim K. Said,[1] and Abdel G. Kafafi[3]

[1]Department of Environmental Health, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, MD 21205 USA; [2]National Institute of Standards and Technology, Chemical Kinetics and Thermodynamics Division, Gaithersburg, MD 20899 USA; [3]Dynex International Inc., Oakville, Ontario L6M 2M7 Canada

A new thermodynamic model for calculating the dissociation constants of complexes formed between the aryl hydrocarbon receptor (AhR) and polychlorinated biphenyls (PCBs) is reported. The free energies of binding of PCBs to AhR are controlled by their lipophilicities, electron affinities, and entropies. The corresponding physicochemical properties of polychlorinated dibenzo-*p*-dioxins and dibenzofurans also control their interactions with AhR. We present evidence supporting the hypothesis that the majority of PCBs are likely to interact with AhR in their nonplanar conformations. In addition, we demonstrate that the affinities of PCBs for AhR relative to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin correlate with corresponding toxic equivalency factors in animals. The reported methodology is likely to be applicable to other polyhalogenated and mixed polyhalogenated bi- and terphenyls and related xenobiotics; thus, it could minimize the number of *in vivo* studies in laboratory animals and facilitate the identification of potentially hazardous aromatic xenobiotics.
Key words: aryl hydrocarbon receptor, binding affinity, polychlorinated biphenyls, structure–activity relationships, toxic equivalency factors. *Environ Health Perspect* 101:422–428(1993)

Polyhalogenated aromatic xenobiotics, such as polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs), and biphenyls (PCBs), are industrial chemicals that elicit a broad spectrum of biologic and toxic responses in animals (*1–10*). It is well established that a key step in the biological and toxicological responses of these classes of xenobiotics in animals is mediated through binding to a common cytosolic protein called the aryl hydrocarbon receptor (AhR) (*1–5*).

The AhR is an intracellular protein whose three-dimensional structure and endogenous ligand are unknown. The receptor mediates the induction of P450IA1, P450IA2, and related enzymes such as aryl hydrocarbon hydroxylase (AHH) and 7-ethoxyresorufin-*O*-deethylase (EROD), as well as several toxic endpoints of polyhalogenated aromatics (*1–10*). Although the cytosolic protein was initially identified in the liver of mice and rats, AhR is not confined to this organ in animals. Several extrahepatic tissues in most mammals, including humans, contain detectable amounts of the protein (*4,5,7,8*). In general, any tissue of a mammalian species containing high concentrations of the receptor has been shown to be an important target for polyhalogenated aromatic toxicity.

Several classical structure–activity relationship (SAR) studies on AhR binding to polyhalogenated aromatic as well as corresponding biological (e.g., enzyme induction) and toxicological processes controlled by the receptor have been reported (*1,3,4, 7–12*). Poland et al. (*1,3*) demonstrated that binding affinities of several PCDDs and PCDFs correlated well with their potencies as AHH inducers in animals. Subsequent work by Safe and co-workers (*4,8,9*) indicated that within each class of aromatic xenobiotics, there is poor linear correlation between AhR binding and corresponding AHH induction potencies. In addition, Safe et al. (*4,9*) showed that ligand width, hydrogen bonding capacity, lipophilicity, and electron-withdrawing effects of substituents seem to be key determinants of the binding process.

Cheney and Tolly (*10*) and McKinney and Singh (*11*), on the basis of *ab initio* quantum mechanical calculations on a number of polyhalogenated aromatics, suggested that binding to AhR is facilitated by an aromatic ring system for which molecular size and planarity are not critical but may affect the strength of binding and that molecular polarizability and electron-accepting properties of the ligand seem to be important in binding. The above correlations were recently confirmed by Rannug et al. (*12*) using computer-automated structure-evaluation programs. However, it is well known that classical SARs suffer from two serious drawbacks: 1) The treatment relies mainly on empirical parameters in its formulation, such as substituent width, hydrogen bonding capacity, and empirical steric parameters, and 2) the multiple regression equations that relate the empirical structural descriptors of xenobiotics to biological activities have limited applicabilities. For example, the regression equation derived for estimating the binding affinities of PCDDs to AhR in rat liver cannot be applied to PCDFs interacting with the same cytosol (*4,7,9*). The latter difficulty is known as the cross-class comparison problem. Therefore, classical approaches to AhR binding and AhR-mediated biological and toxicological responses will remain incomplete without an understanding of the electronic and thermodynamic aspects of these processes.

Using a different approach, Kafafi et al. (*13–15*) developed a new methodology for AhR binding based on electron affinities, entropies, and lipophilicities of the ligands. These quantities are important physicochemical properties that control the interaction between aromatic xenobiotics and AhR, as quantified by the AhR–ligand complex dissociation constant. Unlike traditional studies, Kafafi et al.'s methodology eliminated the majority of empirical structural parameters and multiple regression analysis in its formulation, reliably quantified the affinities of PCDDs and PCDFs for AhR, explained the results of *in vitro* binding studies in a physically consistent way, and eliminated the cross-class comparison problem inherent to classical studies. Furthermore, Kafafi et al. (*15*) were able to establish quantitative relationships between receptor binding avidities of PCDDs and PCDFs and corresponding AHH and EROD enzyme induction potencies.

PCBs are nonplanar, aromatic xenobiotics that are not structurally related to PCDDs and PCDFs, yet some of these compounds bind to AhR effectively and produce biologic and toxicologic responses

Address correspondence to S. A. Kafafi, Department of Environmental Health Sciences, School of Hygiene and Public Health, Johns Hopkins University, 615 North Wolfe Street, Baltimore, MD 21205 USA.
This research was supported by the U.S. Environmental Protection Agency (R-817056-010). We thank the Johns Hopkins University School of Public Health Computer Center for the allocated computer time and the staff of Dynex International Inc. for their assistance in performing the computations. Certain commercial equipment, instruments, or computer programs are identified in this paper to adequately specify the research work. Such identification does not imply recognition or endorsement by the National Institute of Standards and Technology, nor does it imply that the programs or equipment identified are the best available for the purpose.
Received 20 April 1993; accepted 22 June 1993.

characteristic of planar PCDDs and PCDFs. To date, classical structure–activity studies could describe the interaction of PCBs with the cytosolic protein from only a qualitative point of view. That is, PCB–AhR dissociation constants could not be predicted using the traditional approach. Knowledge of these binding affinities is important because it enables us to rank the relative toxicities of congeners, is useful for estimating the corresponding toxic equivalency factors (*8*), and is crucial for understanding the nature of the receptor ligand binding site(s).

In this report we apply the model developed by Kafafi et al. (*13–15*) to estimate the affinities of PCBs for rat hepatic AhR. We show that electron affinities, lipophilicities, and entropies of PCBs are key properties that control their interaction with the cytosolic protein. In addition, we demonstrate that there is a strong correlation between the affinities of PCBs for AhR relative to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and corresponding toxic equivalency factors in animals.

The numbering of PCBs in this paper follows the convention adopted by the International Union of Pure and Applied Chemistry (Fig. 1).

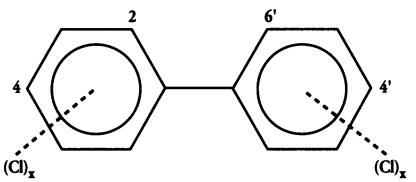

Figure 1. Numbering system used for polychlorinated biphenyls.

Computational Methods

In this section, we briefly describe the computational methods used to estimate lipophilicity (L) as quantified by the octanol–water partition coefficient, electron affinities, and entropies of PCBs (*13–25*).

Octanol–water partition coefficients of PCBs can be estimated from the Hansch and Leo group-additivity method (*16*). The logarithm of octanol–water partition coefficient (log L) of biphenyl used here is 3.90 (*17*). The incremental increase of log L due to Cl substitutions in *ortho*, *meta*, and *para* positions of biphenyl are 0.20, 0.60, and 0.60 log unit/Cl atom, respectively. These increments gave the best log L estimates of PCBs (*17,18*). It is interesting to note that unlike PCDDs and PCDFs (*13–15*), the lipophilicities of PCBs do not vary in a regular way as the number of Cl substituents attached to biphenyl increase. We calculated the electron affinities (EA) and entropies (S) of PCBs from the results of *ab initio* symmetry constrained geometry optimizations using the HF/STO-3G level of theory (*19,20*), as described elsewhere (*13–15,22–25*).

Results and Discussion

Affinities of PCBs for AhR

The results of previous experimental and theoretical studies lead to the conclusion that the interaction between polyhalogenated aromatics and the AhR is of the stacking type, as in charge-transfer complexes where some electronic–charge is transferred from the protein to the ligand (*4,7–11,13–15*). The latter finding is based on the observation that binding affinities of aromatic xenobiotics to the cytosolic protein correlate with electron affinities of ligands. Accordingly, consider the case of two PCBs, which we denote PCB_1 and PCB_2, at equilibrium with their AhR complexes, AhR–PCB_1 and AhR– PCB_2, respectively. The equation describing this reaction and the corresponding equilibrium constant, K, are given by

$$\text{AhR–PCB}_1 + \text{PCB}_2 \rightleftharpoons \text{AhR–PCB}_2 + \text{PCB}_1$$
$$K = K_1/K_2 \qquad (1)$$

where K_1 and K_2 are the dissociation contants of AhR–PCB_1 and AhR–PCB_2 complexes, respectively. Assuming that PCB_1 is 3,3′,4,4′-tetrachlorobiphenyl (TCB) and PCB_2 is any other congener in the class, we can show that (*13,14*):

$$K_{(PCB)} = [L_{(PCB)}/L_{(TCB)}]\, K_{(TCB)} \exp(\Delta S/R) \exp(\Delta EA/RT). \qquad (2)$$

ΔEA and ΔS are given by Equations 3 and 4, respectively:

$$\Delta EA = (EA_{TCB} - EA_{PCB}) \qquad (3)$$

$$\Delta S = (S_{PCB} - S_{TCB}) \qquad (4)$$

The dissociation constants of AhR–PCB complexes computed from Equation 2 are given in the appendix with the corresponding *in vitro* complexes in parentheses (*8,9*). As shown in the appendix, the agreement between experimental and calculated affinities for rat hepatic AhR is fairly good. In addition, from Figure 2, it is clear that the model overcomes cross-class comparison problems of classical SARs because the plot of -ln $K_{(experimental)}$ against -ln $K_{(calculated)}$ for PCDDs, PCDFs, and PCBs is a straight line whose slope is close to unity and nearly passes by the origin (*13,14*). Therefore, we conclude that lipophilicities, electron affinities, and entropies of polyhalogenated aromatics are key electronic and thermodynamic descriptors of their affinities for AhR.

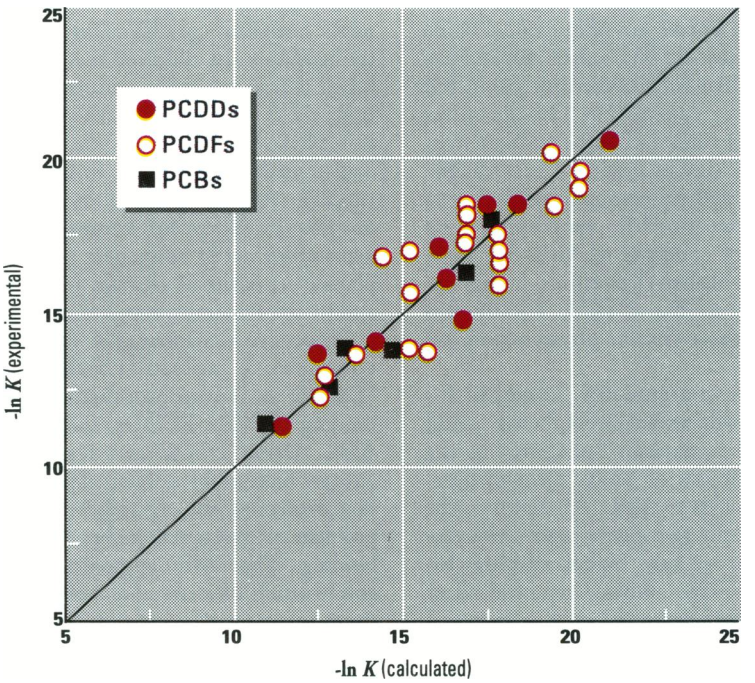

Figure 2. Plot of -ln $K_{(experimental)}$ against - ln $K_{(calculated)}$ for PCBs, PCDDs, and PCDFs ($y = 1.11 + 0.96\,x$; $R = 0.96$).

The model explains the origin of *in vitro* binding studies on PCBs and related xenobiotics (*13–15*). From Equations 2–4, it is clear that a PCB is expected to have higher affinity for the cytosolic protein than TCB (congener 77) if it has a lower L, higher EA, and smaller S. Mono-, di-, and trichlorobiphenyls have lower L,

EA, and *S* values than TCB. For these compounds, *L* and ΔS are expected to cooperatively lower the dissociation constants, whereas ΔEA raises it. ΔEA dominates the interaction with AhR, thus causing mono-, di-, and trichlorobiphenyls to have lower affinities for AhR compared to TCB (see appendix). In addition, as shown in the appendix, non-*ortho*-chlorinated congeners have the highest affinities for the cytosolic protein among these compounds because of their high electron affinities. The latter observation conforms well with the fact that *meta*- and *para*-chlorinated biphenyl–AhR complexes have lower dissociation constants than *ortho*-chlorinated ones (*8,9,12–14*).

All tetrachlorobiphenyls containing *ortho* -Cl atoms, congeners 40–76, have smaller *L*, EA, and *S* values than TCB (congener 77). For these species, ΔEA still controls the interaction of individual PCBs with AhR; that is why isomers 40–76 have lower affinities for the receptor compared to TCB (see appendix). On the other hand, non-*ortho*-polychlorinated biphenyls, 77–81, have similar *L* values. Accordingly, EA and *S* of these compounds determine their affinities for AhR. Furthermore, the dissociation constant of AhR–3,4,4′,5-tetrachlorobiphenyl complex (congener 81) is equal to that of TCB. Clearly, this is due to their similar physicochemical properties.

The above arguments developed for mono through tetrachlorobiphenyls could be applied to explain the trends in the binding affinities of penta- through decachlorobiphenyls to AhR. As shown in the appendix, only two penta- and one hexachlorobiphenyl have higher affinities for AhR than TCB. Notice that the latter congeners are substituted only in *meta* and *para* positions.

In summary, the reported methodology on binding of PCBs to AhR is in agreement with corresponding results from *in vitro* measurements (*8,9*). The most active PCBs are substituted in both *para* and two or more of the *meta* positions. In addition, *ortho* substituents lower the affinities of corresponding compounds for the cytosolic protein.

Unlike PCDDs and PCDFs, the results of our *ab initio* computations on PCBs, as well as those reported by others (*11*), show that biphenyl and its 209 chlorinated congeners are nonplanar. The nonplanarity of these compounds is due to nonbonding repulsion between nearest neighboring *ortho* substituents. The computed barriers to internal rotation in biphenyl and non-*ortho*-polychlorinated congeners are similar, about 1.0–2.0 kcal/mol. Therefore, at room temperature, these compounds can achieve planarity (*11*). On the other hand, the rotational barrier increases to 60 kcal/mol upon introducing the first *ortho* -Cl atom into biphenyl. Additional substitution of corresponding hydrogens by chlorine atoms raise the barriers to internal rotation above 100 kcal/mol; that is, the magnitude of the rotational barrier is comparable to the strength of the carbon–carbon single bond connecting the two aromatic rings. Therefore, it is unlikely that *ortho*-PCBs could achieve planar conformations at room temperature. Accordingly, contrary to the notions advanced by traditional structure–activity models (*8,9*), mono- through tetra-*ortho* -polychlorinated biphenyls are likely to interact with AhR in their nonplanar minimum energy conformations. The latter observation is in agreement with the hypothesis of McKinney and Singh (*11*), who suggested that planarity of ligands is not a necessary condition for binding to the receptor. In addition, it is well established that in molecules with internal rotations about single bonds in the gas or solution phase, these motions become highly constrained upon binding to bioreceptors (*26,27*). Accordingly, the lower affinities of *ortho* -PCBs for AhR compared to non-*ortho*-chlorinated congeners are best explained in terms of changes in electronic and thermodynamic properties of ligands.

Recently, McKinney et al. (*28,29*) used comparative molecular field analysis (CMFA) to develop quantitative SARs for binding of PCBs, PCDDs, and PCDFs to AhR. Using TCDD as a template, the authors successfully developed an approach that overcomes the cross-class comparison problem of traditional studies for receptor binding. The CMFA approach, which is a combination of steric and molecular electrostatic potentials of ligands, parallels the reported methodology in its general predictions for AhR binding to PCBs, PCDDs, and PCDFs. For example, lateral chlorine substitution of aromatic moieties gave favorable electrostatic and steric fields for interaction with AhR. Our model predicts that lateral chlorine atoms increase the electron affinities of corresponding ligands more than longitudinal ones, and this leads to high-affinity binding to AhR. However, Waller and McKinney (*29*) found that the electrostatic and steric field parameters are linearly dependent, and the exclusion of either term significantly affected the performance of their model. In addition, they further noticed that the inclusion of a lipophilicity term in their approach decreased the predicitive capability of their model (*29*). Because our methodology does not use multiple regression analysis in its formulation, the linear dependence of thermodynamic descriptors does not represent any difficulty (*13–15*). Furthermore, lipophilicity is already included in our approach; thus, the reported model could be expanded to predict enzyme induction potencies and *in vivo* toxicities of halogenated aromatics in animals (*15*).

Other approaches for binding of aromatic xenobiotics to AhR based on electrostatic potentials of ligands have been developed (*30,31*). Similar to the above arguments, we can show the paralellism between these models and the reported methodology.

Is there a relationship between the affinities of PCBs for AhR relative to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and corresponding relative toxicities? We discuss this question in the next section.

Relative Toxicities of PCBs

The results of numerous experimental studies on laboratory animals have shown that polyhalogenated aromatics produce similar patterns of biochemical and toxic responses in animals (*1–10,32,33*). The majority of aromatic xenobiotics seem to show the same order of species sensitivity and a similar pattern of biochemical and toxic responses in mammals. These observations prompted scientists and regulatory agencies to develop a relative toxicity scale called the toxic equivalency factor (TEF) (*8*). Because TCDD is the most toxic member, it is assigned a TEF value equal to 1. TEFs of halogenated aromatics are then assigned relative to TCDD based on data from AhR binding, long-term carcinogenicity studies, immunotoxicity, acute lethality, enzyme induction bioassays, etc. As discussed recently by Safe (*8:* 62), "a complete set of data are available only for TCDD and therefore, the assignment of TEFs for halogenated aromatics requires a subjective assessment of the results in which the response priorities will be a contributing factor." The appendix shows our estimated TEFs of PCBs based on orders-of-magnitude affinities for AhR relative to TCDD. The room temperature dissociation constant of AhR–TCDD complex is approximately 1.0×10^{-10} (*8*). TEFs given in the appendix conform fairly well with available values based on results from *in vitro* and *in vivo* experiments on laboratory animals (*8,10,32,33*).

As shown in the appendix, mono- through 2',3,4,5-tetrachlorobiphenyl, congeners 1–76, have estimated TEFs more than 1 million times lower than TCDD. In addition, given the fact that the latter congeners are easily metabolized and excreted by animals (*32,33*), it is unlikely that PCBs 1–76 could be toxic to animals. TEFs of tetrachlorobiphenyls 77 through 81 are predicted to be 1,000–10,000 times less toxic than TCDD, in agreement with

available TEFs based on *in vivo* and *in vitro* experiments (*8*).

Penta- and hexachlorobiphenyls, congeners 82–169, are moderately chlorinated compounds. As shown in the Appendix, the majority of these congeners have TEFs at least 1 million times lower than TCDD, and thus are unlikely to be toxic (*8,32,33*). On the other hand, the most potent penta- and hexachlorobiphenyls are those with TEFs in the range 10–10,000 times less than TCDD (congeners 105, 114, 118, 123, 126, 127, 156, 157, 159, 167, and 169). It is interesting to note that some of the latter congeners have chlorine atoms in *ortho* positions of 3,3',4,4',5,5'-chlorinated biphenyls (see appendix). Furthermore, 3,3',4,4',5,5'-hexachlorobiphenyl, congener 169, is the most potent PCB in the class and has an estimated TEF equal to 0.1. The corresponding value based on results of *in vivo* and *in vitro* experiments is 0.05 (*8*). Accordingly, PCB 169 is expected to show the whole spectrum of TCDD toxic endpoints in animals, possibly with comparable potency.

The heavily chlorinated hepta- through decachlorobiphenyls, congeners 170–209, are expected to be poorly metabolized by most animal species (*32,33*). The most toxic compounds in this group are 170, 180, 189–191, 194, and 205. The corresponding TEFs range from 1,000 to 100,000 times less than TCDD, in agreement with corresponding values based on experimental data (*8*). However, it must be noted that octa- through decachlorobiphenyls were never detected in environmental samples due to their high lipophilicities (*32*). From the above discussion we conclude that for any class of polyhalogenated and mixed polyhalogenated bi- and terphenyls, the reported model for AhR binding could be useful for estimating orders of magnitude TEFs. Therefore, it could greatly minimize the necessity for large numbers of *in vivo* studies on laboratory animals and facilitate the identification of potentially hazardous polyhalogenated and mixed polyhalogenated aromatic xenobiotics in animals. In a future publication, we will apply the developed methodologies to polycyclic aromatic hydrocarbons and other AhR mediated processes.

References

1. Poland A, Glover E, Kende AS. Stereospecific high binding affinity of 2,3,7,8-tetrachlorodibenzo-p-dioxin by hepatic cytosols. Evidence that the binding species is a receptor for induction of aryl hydrocarbon hydroxylase. J Biol Chem 251:4936–4946(1976).
2. Nebert DW. The Ah locus: genetic differences in toxicity, cancer, mutation, and birth defects. Toxicology 20:153–174(1989).
3. Poland A, Knutson JC. 2,3,7,8-Tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: examination of the mechanism of toxicity. Annu Rev Pharmacol Toxicol 22:517–554(1982).
4. Safe S. Comparative toxicology and mechanism of action of polychlorinated dibenzo-p-dioxins and dibenzofurans. Annu Rev Pharmacol Toxicol 26:371–399(1986).
5. Gallo MA, Scheuplein RJ, Van Der Heijden KA, eds. Biological basis for risk assessment of dioxins and related compounds. Banbury Report 35. Cold Spring Harbor, NY:Cold Spring Harbor Laboratory Press, 1991.
6. Waid JS, ed. PCBs and the environment, vols 1–3. Boca Raton, FL:CRC Press, 1986.
7. Okey AB. Enzyme induction in the cytochrome P-450 system. Pharmacol Ther 45: 241–298(1990).
8. Safe S. Polychlorinated biphenyls (PCBs), dibenzo-p-dioxins (PCDDs), dibenzofurans (PCDFs), and related compounds: environmental and mechanistic considerations which support the development of toxic equivalency factors (TEFs). Crit Rev Toxicol 21:51–88 (1990).
9. Safe S, Bandiera S, Sawyer T, Bozena Z, Mason G, Romkes M, Denomme M, Sparling J, Okey AB, Fujita T. Effects of structure on binding to the 2,3,7,8-TCDD receptor protein and AHH induction—halogenated biphenyls. Environ Health Perspect 61:21–33(1985).
10. Cheney BV, Tolly T. Electronic factors affecting receptor binding of dibenzo-p-dioxins and dibenzofurans. Int J Quant Chem 16:87–110(1979).
11. McKinney JD, Singh P. Structure-activity relationships in halogenated biphenyls: unifying hypothesis for structural specifity. Chem-Biol Interact 33:271(1981).
12. Rannug A, Sjogren M, Rannug A, Gillner M, Toftgard R, Gustafsson JA, Rosenkranz H, Klopman G. Use of artificial intelligence in structure-affinity correlations of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) receptor ligands. Carcinogenesis 12:2007–2015(1991).
13. Kafafi SA, Afeefy HY, Said HK, Hakimi JM. A new structure-activity model for Ah receptor binding. Polychlorinated dibenzo-p-dioxins and dibenzofurans. Chem Res Toxicol 5:856–862(1992).
14. Kafafi SA, Said HK, Mahmoud MI, Afeefy HY. The electronic and thermodynamic aspects of Ah receptor binding. A new structure-activity model: I. The polychlorinated dibenzo-p-dioxins. Carcinogenesis 13:1599–1605(1992).
15. Kafafi SA, Afeefy HY, Said HK, Kafafi AG. Relationship between aryl hydrocarbon receptor binding, induction of aryl hydrocarbon hydroxylase and 7-ethoxyresorufin-O-deethylase enzymes and toxic activities of aromatic xenobiotics in animals. A new model. Chem Res Toxicol 6:328–334(1993).
16. Hansch C, Leo A. Substituent constants for correlation analysis in chemistry and biology. New York:Wiley-Interscience, 1979.
17. Chessells M, Hawker DW, Connell DW. Critical evaluation of the measurement of the 1-octanol/water partition coefficient of hydrophobic compounds. Chemosphere 22:175–119(1991).
18. Risby TH, Hsu T, Sehnert SS, Bhan P. Physicochemical parameters of individual hexachlorobiphenyl congeners. Environ Sci Tech 24:1680–1687(1990).
19. Binkley JS, Frisch MJ, DeFrees DJ, Raghavachari K, Whiteside RA, Schlegel HB, Fluder EM, Pople JA. Gaussian 86. Pittsburgh, PA:Carnegie-Mellon University, 1986.
20. Hehre WJ, Radom L, Schleyer PvR, Pople JA. Ab initio molecular orbital theory. New York:John Wiley and Sons, 1986;26–132.
21. Kebarle P, Chowdhury S. Electron affinities and electron transfer reactions. Chem Rev 87:513–534(1987).
22. Benson SW. Thermochemical kinetics. Methods for the estimation of thermochemical data and rate parameters. New York: John Wiley and Sons,1976.
23. Lias SG, Bartmess JE, Liebman JF, Holmes JL, Levin RD, Mallard WG. Gas-phase ion and neutral thermochemistry. J Phys Chem Ref Data 17:1–39(1988).
24. Kafafi SA, Lowe JP. Substitutional effects on polymer band gaps. In: From atoms to polymers: isoelectronic analogies (Liebman JF, Greenberg A, eds). New York:VCH Publishers, 1989;279–305.
25. Kafafi SA, LaFemina JP, Nauss JL. Electronic structure and conformation of polymers from cluster molecular orbital and molecular mechanics calculations. J Am Chem Soc 112:8742–8746(1990).
26. Searle MS, Williams DH. The cost of conformational order: entropy changes in molecular associations. J Am Chem Soc 114:10690–10697(1992).
27. Searle MS, Williams DH, Gerhard U. Partitioning of free energy contributions in the estimation of binding constants: residual motions and consequences for amide-amide hydrogen bond strengths. J Am Chem Soc 114:10697–10704(1992).
28. McKinney JD, Darden T, Lyerly MA, Pederson LG. PCB and related compound binding to the Ah receptor(s). Theoretical model based on molecular parameters and molecular mechanics. Quant Struct-Act Relat 4:166–172 (1985).
29. Waller CL, McKinney JD. Comparative molecular field analysis of polyhalogenated dibenzo-p-dioxins, dibenzofurans and biphenyls. J Med Chem 35:3660–3666(1992).
30. Politzer P, Laurence PR, Jayasuriya K. Molecular electrostatic potentials: an effective tool for the elucidation of biochemical phenomena. Environ Health Perspect 61:191–202(1985).
31. Sjoberg P, Murray JS, Brinck T, Evans P, Politzer P. The use of electrostatic potential at the molecular surface in recognition interactions: dibenzo-p-dioxins and related systems. J Mol Graphics 8:81–90(1990).
32. McFarland VA, Clarke JU. Environmental occurrence, abundance, and potential toxicity of polychlorinated biphenyl congeners: considerations for a congener-specific analysis. Environ Health Perspect 81:225–239(1989).
33. Birnbaum L. The role of structure in the disposition of halogenated aromatic xenobiotics. Environ Health Perspect 61:11–20(1985).

Appendix. Calculated lipophilicities (L), electron affinities (EA), and entropies (S) of PCBs relative to 3,3',4,4'-tetrachlorobiphenyl, *in vitro* dissociation constants (K) of PCB-AhR complexes in rat liver cytosols, and toxic equivalency factors (TEF)

No.	PCB	L/L_{TCB}	ΔEA (ev)	ΔS (cal/mol·K)	$K_{(calc)}$(M)[a]	TEF[b]
Monochlorobiphenyls						
1	2-B	0.0063	0.70	-21.62	7.1×10^{-2}	10^{-9}
2	3-B	0.016	0.55	-19.62	8.4×10^{-4}	10^{-7}
3	4-B	0.016	0.50	-19.62	9.9×10^{-5}	10^{-6}
Dichlorobiphenyls						
4	2,2'-B	0.010	0.70	-18.00	0.69	10^{-10}
5	2,3-B	0.025	0.55	-14.62	1.6×10^{-2}	10^{-8}
6	2,3'-B	0.025	0.55	-14.62	1.6×10^{-2}	10^{-8}
7	2,4-B	0.025	0.50	-14.62	1.9×10^{-3}	10^{-7}
8	2,4'-B	0.025	0.50	-14.62	1.9×10^{-3}	10^{-7}
9	2,5-B	0.025	0.55	-14.62	1.6×10^{-2}	10^{-8}
10	2,6-B	0.010	0.70	-18.00	0.69	10^{-10}
11	3,3'-B	0.063	0.40	-14.00	9.4×10^{-5}	10^{-6}
12	3,4-B	0.063	0.35	-12.62	2.3×10^{-5}	10^{-5}
13	3,4'-B	0.063	0.35	-12.62	2.3×10^{-5}	10^{-5}
14	3,5-B	0.063	0.40	-14.00	9.4×10^{-5}	10^{-6}
15	4,4'-B	0.063	0.30	-14.00	1.3×10^{-6}	10^{-4}
Trichlorobiphenyls						
16	2,2',3-B	0.040	0.55	-9.62	0.32	10^{-10}
17	2,2',4-B	0.040	0.50	-9.62	3.8×10^{-2}	10^{-8}
18	2,2',5-B	0.040	0.55	-9.62	0.32	10^{-10}
19	2,2',6-B	0.016	0.70	-9.62	75.2	10^{-12}
20	2,3,3'-B	0.10	0.40	-7.62	3.7×10^{-4}	10^{-6}
21	2,3,4-B	0.10	0.35	-7.62	4.4×10^{-4}	10^{-6}
22	2,3,4'-B	0.10	0.35	-7.62	4.4×10^{-4}	10^{-6}
23	2,3,5-B	0.10	0.40	-7.62	3.7×10^{-4}	10^{-6}
24	2,3,6-B	0.040	0.55	-7.62	0.88	10^{-10}
25	2,3',4-B	0.10	0.35	-7.62	4.4×10^{-4}	10^{-6}
26	2,3',5-B	0.10	0.40	-7.62	3.7×10^{-4}	10^{-6}
27	2,3',6-B	0.040	0.55	-7.62	0.88	10^{-10}
28	2,4,4'-B	0.10	0.30	-7.62	5.3×10^{-5}	10^{-6}
29	2,4,5-B	0.10	0.35	-7.62	4.4×10^{-4}	10^{-6}
30	2,4, 6-B	0.040	0.50	-9.00	5.2×10^{-2}	10^{-9}
31	2,4',5-B	0.10	0.35	-7.62	4.4×10^{-4}	10^{-6}
32	2,4',6-B	0.040	0.50	-9.00	5.2×10^{-2}	10^{-7}
33	2',3,4-B	0.10	0.35	-7.62	5.3×10^{-5}	10^{-6}
34	2',3,5-B	0.10	0.40	-7.62	3.7×10^{-4}	10^{-6}
35	3,3',4-B	0.25	0.20	-5.62	5.1×10^{-6}	10^{-5}
36	3,3',5-B	0.25	0.25	-5.62	4.3×10^{-5}	10^{-6}
37	3,4,4'-B	0.25	0.15	-5.62	6.0×10^{-7}	10^{-4}
38	3,4,5-B	0.25	0.20	-7.00	2.5×10^{-6}	10^{-4}
39	3,4',5-B	0.25	0.20	-7.00	2.5×10^{-6}	10^{-4}
Tetrachlorobiphenyls						
40	2,2',3,3'-B	0.16	0.40	-4.00	3.7×10^{-2}	10^{-9}
41	2,2',3,4-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
42	2,2',3,4'-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
43	2,2',3,5-B	0.16	0.40	-2.62	7.4×10^{-2}	10^{-9}
44	2,2',3,5'-B	0.16	0.40	-2.62	7.4×10^{-2}	10^{-9}
45	2,2',3,6-B	0.063	0.55	-4.62	6.3	10^{-11}
46	2,2',3,6'-B	0.063	0.55	-4.62	6.3	10^{-11}
47	2,2',4,4'-B	0.16	0.30	-4.00	5.2×10^{-4} (1.3×10^{-4})[c]	10^{-7}
48	2,2',4,5-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
49	2,2',4,5'-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
50	2,2',4,6-B	0.063	0.50	-4.62	0.74	10^{-10}
51	2,2',4,6'-B	0.063	0.50	-4.62	0.74	10^{-10}
52	2,2',5,5'-B	0.16	0.40	-4.00	3.7×10^{-2}	10^{-8}
53	2,2',5,6'-B	0.063	0.55	-4.62	6.3	10^{-11}
54	2,2',6,6'-B	0.025	0.70	-9.37	133.4	10^{-13}
55	2,3,3',4-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
56	2,3,3',4'-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
57	2,3,3',5-B	0.40	0.25	-0.62	8.6×10^{-4}	10^{-7}
58	2,3,3',5'-B	0.40	0.25	-0.62	8.6×10^{-4}	10^{-7}
59	2,3,3',6-B	0.16	0.40	-2.62	7.4×10^{-2}	10^{-9}
60	2,3,4,4'-B	0.40	0.15	-2.62	4.4×10^{-6} (2.8×10^{-6})	10^{-5}
61	2,3,4,5-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
62	2,3,4,6-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
63	2,3,4',5-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
64	2,3,4',6-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
65	2,3,5,6-B	0.16	0.40	-4.00	3.7×10^{-2}	10^{-8}
66	2,3',4,4'-B	0.40	0.15	-2.62	4.4×10^{-6} (2.8×10^{-6})	10^{-5}
67	2,3',4,5-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
68	2,3',4,5'-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
69	2,3',4,6-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}

No.	PCB	L/L_{TCB}	ΔEA (ev)	ΔS (cal/mol-K)	$K_{(calc)}$(M)[a]	TEF[b]
70	2,3',4',5-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
71	2,3',4',6-B	0.16	0.35	-2.62	8.8×10^{-3}	10^{-8}
72	2,3',5,5'-B	0.40	0.25	-0.62	8.6×10^{-4}	10^{-7}
73	2,3',5',6-B	0.16	0.40	-2.62	7.4×10^{-2}	10^{-9}
74	2,4,4',5-B	0.40	0.15	-2.62	4.4×10^{-6} (2.8×10^{-6})	10^{-5}
75	2,4,4',6-B	0.16	0.30	-4.00	5.2×10^{-4}	10^{-7}
76	2',3,4,5-B	0.40	0.20	-0.62	1.0×10^{-4}	10^{-6}
77	3,3',4,4'-B	1.00	0.00	0.00	7.1×10^{-8} (7.1×10^{-8})	10^{-3} (0.01)
78	3,3',4,5-B	1.00	0.05	1.38	1.1×10^{-6}	10^{-4}
79	3,3',4,5'-B	1.00	0.05	1.38	1.1×10^{-6}	10^{-4}
80	3,3',5,5'-B	1.00	0.10	-1.38	2.4×10^{-6}	10^{-4}
81	3,4,4',5-B	1.00	0.00	0.00	7.1×10^{-8} (7.1×10^{-8})	10^{-3}
Pentachlorobiphenyls						
82	2,2',3,3',4-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
83	2,2',3,3',5-B	0.63	0.25	4.38	1.7×10^{-2}	10^{-8}
84	2,2',3,3',6-B	0.25	0.40	2.38	1.4	10^{-10}
85	2,2',3,4,4'-B	0.63	0.15	4.38	2.4×10^{-4}	10^{-6}
86	2,2',3,4,5-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
87	2,2',3,4,5'-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
88	2,2',3,4,6-B	0.25	0.35	2.38	0.17	10^{-10}
89	2,2',3,4,6'-B	0.25	0.35	2.38	0.17	10^{-10}
90	2,2',3,4',5-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
91	2,2',3,4',6-B	0.25	0.35	2.38	0.17	10^{-10}
92	2,2',3,5,5'-B	0.63	0.25	4.38	1.7×10^{-2}	10^{-8}
93	2,2',3,5,6-B	0.25	0.40	2.38	1.4	10^{-10}
94	2,2',3,5,6'-B	0.25	0.40	2.38	1.4	10^{-10}
95	2,2',3,5',6-B	0.25	0.40	2.38	1.4	10^{-10}
96	2,2',3,6,6'-B	0.10	0.55	0.38	122.5	10^{-13}
97	2,2',3',4,5-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
98	2,2',3',4,6-B	0.25	0.35	2.38	0.17	10^{-10}
99	2,2',4,4',5-B	0.63	0.15	4.38	2.4×10^{-4}	10^{-6}
100	2,2',4,4',6-B	0.25	0.30	2.38	2.0×10^{-2}	10^{-8}
101	2,2',4,5,5'-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
102	2,2',4,5,6'-B	0.25	0.35	2.38	0.17	10^{-10}
103	2,2',4,5',6-B	0.25	0.35	2.38	0.17	10^{-10}
104	2,2',4,6,6'-B	0.10	0.50	-1.00	7.3	10^{-11}
105	2,3,3',4,4'-B	1.59	0.00	6.38	2.7×10^{-6} (6.9×10^{-7})	10^{-4} (0.001)
106	2,3,3',4,5-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
107	2,3,3',4',5-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
108	2,3,3',4,5'-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
109	2,3,3',4,6-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
110	2,3,3',4',6-B	0.63	0.20	4.38	2.0×10^{-3}	10^{-7}
111	2,3,3',5,5'-B	1.59	0.10	6.38	2.0×10^{-4}	10^{-6}
112	2,3,3',5,6-B	0.63	0.25	4.38	1.7×10^{-2}	10^{-8}
113	2,3,3',5',6-B	0.63	0.25	4.38	1.7×10^{-2}	10^{-8}
114	2,3,4,4',5-B	1.59	0.00	6.38	2.7×10^{-6} (6.9×10^{-7})	10^{-4} (0.001)
115	2,3,4,4',6-B	0.63	0.15	4.38	2.4×10^{-4}	10^{-6}
116	2,3,4,5,6-B	0.63	0.20	3.00	1.0×10^{-4}	10^{-6}
117	2,3,4',5,6-B	0.63	0.20	3.00	1.0×10^{-4}	10^{-6}
118	2,3',4,4',5-B	1.59	0.00	6.38	2.7×10^{-6} (6.9×10^{-7})	10^{-4} (0.001)
119	2,3',4,4',6-B	0.63	0.15	4.38	2.4×10^{-4}	10^{-6}
120	2,3',4,5,5'-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
121	2,3',4,5',6-B	0.63	0.20	3.00	1.0×10^{-4}	10^{-6}
122	2',3,3',4,5-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
123	2',3,4,4',5-B	1.59	0.00	6.38	2.7×10^{-6} (6.9×10^{-7})	10^{-4} (0.001)
124	2',3,4,5,5'-B	1.59	0.05	6.38	2.3×10^{-5}	10^{-5}
125	2',3,4,5,6'-B	0.63	0.20	3.00	1.4×10^{-5}	10^{-5}
126	3,3',4,4',5-B	3.98	-0.15	8.38	3.3×10^{-8} (1.3×10^{-8})	10^{-2} (0.1)
127	3,3',4,5,5'-B	3.98	-0.10	7.00	1.0×10^{-7}	10^{-3}
Hexachlorobiphenyls						
128	2,2',3,3',4,4'-B	2.51	0.00	10.00	2.7×10^{-5} (8.9×10^{-6})	10^{-5} (0.00002)
129	2,2',3,3',4,5-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
130	2,2',3,3',4,5'-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
131	2,2',3,3',4,6-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
132	2,2',3,3',4,6'-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
133	2,2',3,3',5,5'-B	2.51	0.10	10.00	1.9×10^{-3}	10^{-7}
134	2,2',3,3',5,6-B	1.00	0.25	9.38	0.33	10^{-10}
135	2,2',3,3',5,6'-B	1.00	0.25	9.38	0.33	10^{-10}
136	2,2',3,3',6,6'-B	0.40	0.40	7.38	28.3	10^{-12}
137	2,2',3,4,4',5-B	2.51	0.00	11.38	5.5×10^{-5} (8.9×10^{-6})	10^{-6} (0.00002)
138	2,2',3,4,4',5'-B	2.51	0.00	11.38	5.5×10^{-5} (8.9×10^{-6})	10^{-6} (0.00002)
139	2,2',3,4,4',6-B	1.00	0.15	9.38	4.7×10^{-3}	10^{-8}
140	2,2',3,4,4',6'-B	1.00	0.15	9.38	4.7×10^{-3}	10^{-8}
141	2,2',3,4,5,5'-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
142	2,2',3,4,5,6-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
143	2,2',3,4,5,6'-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}

No.	PCB	I/I_{TCB}	ΔEA (ev)	ΔS (cal/mol-K)	$K_{(calc)}$(M)[a]	TEF[b]
144	2,2′,3,4,5′,6-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
145	2,2′,3,4,6,6′-B	0.40	0.35	7.38	3.4	10^{-10}
146	2,2′,3,4′,5,5′-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
147	2,2′,3,4′,5,6-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
148	2,2′,3,4′,5,6′-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
149	2,2′,3,4′,5′,6-B	1.00	0.20	9.38	3.9×10^{-2}	10^{-8}
150	2,2′,3,4′,6,6′-B	0.40	0.35	7.38	3.4	10^{-10}
151	2,2′,3,5,5′,6-B	1.00	0.25	9.38	0.33	10^{-10}
152	2,2′,3,5,6,6′-B	0.40	0.40	6.00	14.1	10^{-11}
153	2,2′,4,4′,5,5′-B	2.51	0.00	10.00	2.7×10^{-5} (8.9×10^{-6})	10^{-5} (0.00002)
154	2,2′,4,4′,5,6′-B	1.00	0.15	9.38	4.7×10^{-3}	10^{-8}
155	2,2′,4,4′,6,6′-B	0.40	0.30	6.00	0.20	10^{-10}
156	2,3,3′,4,4′,5-B	6.31	-0.15	13.38	6.1×10^{-7} (8.1×10^{-7})	10^{-4} (0.001)
157	2,3,3′,4,4′,5′-B	6.31	-0.15	13.38	6.1×10^{-7} (8.1×10^{-7})	10^{-4} (0.001)
158	2,3,3′,4,4′,6-B	2.51	0.00	11.38	5.5×10^{-5} (8.9×10^{-6})	10^{-6}
159	2,3,3′,4,5,5′-B	6.31	-0.10	13.38	5.3×10^{-6}	10^{-5}
160	2,3,3′,4,5,6-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
161	2,3,3′,4,5′,6-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
162	2,3,3′,4′,5,5′-B	6.31	-0.10	13.38	5.3×10^{-6}	10^{-5}
163	2,3,3′,4′,5,6-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
164	2,3,3′,4′,5′,6-B	2.51	0.05	11.38	4.6×10^{-4}	10^{-7}
165	2,3,3′,5,5′,6-B	2.51	0.10	10.00	1.9×10^{-3}	10^{-7}
166	2,3,4,4′,5,6-B	2.51	0.00	10.00	2.7×10^{-5} (8.9×10^{-6})	10^{-5} (0.00002)
167	2,3′,4,4′,5,5′-B	6.31	-0.15	13.38	6.1×10^{-7} (8.1×10^{-7})	10^{-4} (0.001)
168	2,3′,4,4′,5′,6-B	2.51	0.00	10.00	2.7×10^{-5} (8.9×10^{-6})	10^{-5} (0.00002)
169	3,3′,4,4′,5,5′-B	15.85	-0.30	14.00	3.7×10^{-9} (Insoluble)	10^{-1}(0.05)
Heptachlorobiphenyls						
170	2,2′,3,3′,4,4′,5-B	10.00	-0.15	18.38	1.3×10^{-5}	10^{-5}(0.00002)
171	2,2′,3,3′,4,4′,6-B	3.98	0.00	16.38	1.1×10^{-3}	10^{-7}
172	2,2′,3,3′,4,5,5′-B	10.00	-0.10	18.38	1.1×10^{-4}	10^{-6}(0.00002)
173	2,2′,3,3′,4,5,6-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
174	2,2′,3,3′,4,5,6′-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
175	2,2′,3,3′,4,5′,6-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
176	2,2′,3,3′,4,6,6′-B	1.58	0.20	14.38	0.77	10^{-10}
177	2,2′,3,3′,4′,5,6-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
178	2,2′,3,3′,5,5′,6-B	3.98	0.10	16.38	7.5×10^{-2}	10^{-9}
179	2,2′,3,3′,5,6,6′-B	1.58	0.25	14.38	6.4	10^{-11}
180	2,2′,3,4,4′,5,5′-B	10.00	-0.15	18.38	1.3×10^{-5}	10^{-5} (0.00002)
181	2,2′,3,4,4′,5,6-B	3.98	0.00	16.38	1.1×10^{-3}	10^{-7}
182	2,2′,3,4,4′,5,6′-B	3.98	0.00	16.38	1.1×10^{-3}	10^{-7}
183	2,2′,3,4,4′,5′,6-B	3.98	0.00	16.38	1.1×10^{-3}	10^{-7}
184	2,2′,3,4,4′,6,6′-B	1.58	0.15	14.38	9.2×10^{-2}	10^{-9}
185	2,2′,3,4,5,5′,6-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
186	2,2′,3,4,5,6,6′-B	1.58	0.20	13.00	0.38	10^{-10}
187	2,2′,3,4′,5,5′,6-B	3.98	0.05	16.38	9.0×10^{-3}	10^{-8}
188	2,2′,3,4′,5,6,6′-B	1.58	0.20	13.00	0.38	10^{-10}
189	2,3,3′,4,4′,5,5′-B	25.12	-0.30	18.38	5.2×10^{-8}	10^{-3} (0.001)
190	2,3,3′,4,4′,5,6-B	10.00	-0.15	16.38	4.5×10^{-6}	10^{-5} (0.00002)
191	2,3,3′,4,4′,5′,6-B	10.00	-0.15	16.38	4.5×10^{-6}	10^{-5} (0.00002)
192	2,3,3′,4,5,5′,6-B	10.00	-0.10	17.00	5.3×10^{-5}	10^{-6}
193	2,3,3′,4′,5,5′,6-B	10.00	-0.10	17.00	5.3×10^{-5}	10^{-6}
Octachlorobiphenyls						
194	2,2′,3,3′,4,4′,5,5′-B	39.81	-0.30	25.38	2.7×10^{-6}	10^{-4} (0.00002)
195	2,2′,3,3′,4,4′,5,6-B	15.85	-0.15	23.38	2.5×10^{-4}	10^{-6}
196	2,2′,3,3′,4,4′,5,6′-B	15.85	-0.15	23.38	2.5×10^{-4}	10^{-6}
197	2,2′,3,3′,4,4′,6,6′-B	6.31	0.00	20.00	1.1×10^{-2}	10^{-8}
198	2,2′,3,3′,4,5,5′,6-B	15.85	-0.10	23.38	2.1×10^{-3}	10^{-7}
199	2,2′,3,3′,4,5,6,6′-B	6.31	0.05	21.38	0.18	10^{-10}
200	2,2′,3,3′,4,5′,6,6′-B	6.31	0.05	21.38	0.18	10^{-10}
201	2,2′,3,3′,4,5,5′,6′-B	15.85	-0.10	21.38	7.6×10^{-4}	10^{-7}
202	2,2′,3,3′,5,5′,6,6′-B	6.31	0.10	20.00	0.74	10^{-10}
203	2,2′,3,4,4′,5,5′,6-B	15.85	-0.15	23.38	2.5×10^{-4}	10^{-6}
204	2,2′,3,4,4′,5′,6,6′-B	6.31	0.00	21.38	2.1×10^{-2}	10^{-8}
205	2,3,3′,4,4′,5,5′,6-B	39.81	-0.30	25.38	2.7×10^{-6}	10^{-4} (0.00002)
Nonachlorobiphenyls						
206	2,2′,3,3′,4,4′,5,5′,6-B	63.10	-0.30	30.38	5.5×10^{-5}	10^{-6}
207	2,2′,3,4,4′,5,5′,6,6′-B	25.12	-0.15	28.38	4.8×10^{-3}	10^{-8}
208	2,2′,3,3′,4,5,5′,6,6′-B	25.12	-0.10	28.38	4.0×10^{-2}	10^{-8}
Decachlorobiphenyl						
209	2,2′,3,3′,4,4′,5,5′,6,6′-B	100.00	-0.30	34.00	5.4×10^{-4}	10^{-7}
	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin				1.0×10^{-10}	1

[a]Experimental values from Safe et al (*9*). Similar substitution patterns are averaged.

[b]Experimental values from Safe (*8*).

[c]Experimental values given in parentheses.